

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 5

composition of matter of claim ~~141~~.--

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--~~144~~.

16

(New) A method of imaging prostate cancer in a subject which comprises administering to the subject the composition of matter of claim ~~141~~, wherein the agent is an imaging agent under conditions permitting formation of a complex between the composition of matter and prostate specific membrane antigen, and obtaining an image of any complex so formed.--

#### REMARKS

First, applicants would like to thank Examiner Stephen Gucker for agreeing during an April 30, 2001 telephone conference with Spencer Schneider of the undersigned attorney's office to consider this Substitute Amendment.

Claims 114-118 and 120-127 are pending in the subject application. Applicants have hereinabove canceled claims 114-118 and 120-127 without disclaimer or prejudice to their right to pursue the subject matter of these claims in a later-filed application and added new claims 128-144. Support for this amendment may be found inter alia in the specification as follows: claim 128: corresponds to prior claim 114; page 22, lines 9-12; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 129: corresponds to prior claim 115; page 22, lines 9-12; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 130: corresponds to prior

B2

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 6

claim 116; page 22, lines 9-12; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 131: corresponds to prior claim 117; page 22, lines 9-12; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; page 53, line 20 to page 54, line 7; claim 132: corresponds to prior claim 118; page 22, lines 9-12; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 133: corresponds to prior claim 120; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; page 30, lines 1-11; page 22, lines 10-11; claim 134: corresponds to prior claim 114; page 22, lines 9-12; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 135: corresponds to prior claim 115; page 22, lines 9-12; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 136: corresponds to prior claim 116; page 22, lines 9-12; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 137: corresponds to prior claim 127; page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 138: page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; claim 139: page 31, line 14 to page 32, line 32; page 31, lines 6-12; page 54, lines 4-7; page 30, line 32; page 30, lines 1-11; figure 14-1; page 30, lines 1-11; page 22, lines

1

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 7

10-11; page 17, lines 15-25; claim 140: corresponds to prior claim 122; page 32, lines 16-22; claim 141: corresponds to prior claim 123; page 32, line 34 to page 33, line 26; claim 142: corresponds to prior claim 124; page 32, line 34 to page 33, line 26; claim 143: corresponds to prior claim 125; page 32, line 34 to page 33, line 26; and claim 144: corresponds to prior claim 126; page 32, line 34 to page 33, line 26. This amendment does not involve any issue of new matter. Therefore, entry of this amendment is respectfully requested such that claims 128-144 will be pending.

Rejection under 35 U.S.C. §101

The Examiner rejected claims 114-118 and 120-122 under 35 U.S.C. §101, alleging that the claimed invention is directed to non-statutory subject matter. The Examiner stated that the antibodies claimed are products of nature and do not show the hand of man. The Examiner stated that amending the claims to recite an isolated or purified antibody would obviate this ground of this rejection.

In response, applicants without conceding the correctness of the Examiner's position but to expedite prosecution of the subject application have herein canceled claims 114-118 and 120-127 without disclaimer or prejudice to their right to pursue the subject matter of these claims in a later-filed application and added new claims 144. In accordance with the Examiner's suggestions, new claims 128-139 recite "A purified antibody....." [emphasis added]. Applicants contend that these amendments obviate the above ground of rejection and respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §101.

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 8

Rejection under 35 U.S.C. 112, second paragraph

The Examiner rejected claims 114-118 and 120-126 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner stated that the Examiner was unable to find a definition for "an outside region of" prostate specific membrane antigenic polypeptide in the specification. The Examiner stated that given the disclosure on pages 53-54 of only a membrane spanning domain, an "outside region" could be interpreted as being either the inner or outer membrane domain of the PSM antigen as described on page 54 because either domain is outside of the transmembrane domain which appears to be the only domain specifically identified in the specification, i.e. the Examiner could not find in the instant specification any teachings as to the orientation of the PSM antigen other than the disclosure of a membrane spanning domain. The Examiner stated that given the lack of teaching as to the PSM antigen's orientation in the cell, i.e. to the location of the N-or C-terminal as being intracellular or extracellular, the new limitation of "an outside region of" is vague and indefinite for not distinguishing between the inner and outer membrane domains of PSM antigen. The Examiner stated that the grounds of this rejection could be obviated by amending the claims to correspond to the language of page 54, line 5, which describes "an outer membrane domain[s] of the PSM antigen".

In response, applicants respectfully traverse the Examiner's above rejection because an outside region is clearly synonymous with an outer membrane domain, both of which are synonymous with an extracellular domain. Nevertheless, applicants without conceding

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 9

the correctness of the Examiner's position and without disclaimer or prejudice but to expedite prosecution of the subject application have hereinabove canceled claims 114-118 and 120-127 without disclaimer or prejudice to their right to pursue the subject matter of these claims in a later-filed application and added new claims 128-144. Newly added claims 128-139 recite the term "outer membrane domain" and not "outside region." Applicants contend that this amendment obviates the above ground of rejection and respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, second paragraph..

Rejection under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 114-118 under 35 U.S.C. §112, second paragraph as being vague and indefinite, alleging that these claims recite transitional language which could be interpreted to relate back to the antibody or the PSM antigen. The Examiner stated for instance, in claim 114, the subject of "comprising a fragment of the prostate specific membrane antigen having within its structure..." could be interpreted as either the antibody or the PSM antigen as the claim is currently worded. The Examiner stated that it is suggested that the claims be amended to recite wording along the lines of: An antibody which binds to an outer membrane domain of prostate specific membrane antigenic polypeptide wherein said outer membrane domain comprises a fragment of the prostate specific membrane antigen having within its structure the consecutive amino acid sequence.

In response, applicants respectfully traverse the Examiner's above rejection because an outside region is clearly synonymous with an outer membrane domain, both of which are synonymous with an

1

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 10

extracellular domain. Nevertheless, applicants without conceding the correctness of the Examiner's position and without disclaimer or prejudice but to expedite prosecution of the subject application have hereinabove canceled claims 114-127 without disclaimer or prejudice to their right to pursue the subject matter of these claims in a later-filed application. Although they submit that claims 114-118 were neither vague nor indefinite, applicants contend that it is clear to what the transitional language refers in newly added claims 128-144. Applicants contend that this amendment obviates the above ground of rejection and respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §112, second paragraph.

Rejection under 35 U.S.C. §102(e)

The Examiner rejected claims 114-118 and 120-126 under 35 U.S.C. §102(e) as anticipated by Horoszewicz, which the Examiner alleges discloses 7E11-C5, a monoclonal antibody that binds to PSMA (column 11, lines 27-56 and column 12, lines 31 to column 13, line 12) which meet all the limitations of the instant claims because of the inherency of SEQ ID NO:2 to PSMA. The Examiner stated in addition, the open language of claim 121 and the recitation of the outside region is anticipated by Horoszewicz.

The Examiner stated that applicant's arguments filed February 12, 2001 have been fully considered but they are not persuasive because the Examiner was unable to find a definition for "an outside region of" prostate specific membrane antigenic polypeptide in the specification. The Examiner stated that given the disclosure on pages 53-54 of only a membrane spanning domain, an "outside region"

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 11

could be interpreted as being either inner or outer membrane domain of the PSM antigen as described on page 54 because either domain is outside of the transmembrane domain which appears to be the only domain specifically identified in the specification, i.e. the Examiner could not find in the instant specification any teachings as to the orientation of the PSM antigen other than the disclosure of a membrane spanning domain. The Examiner stated that given the lack of teaching as to the PSM antigen's orientation in the cell, i.e. to the location of the N-or C-terminal as being intracellular or extracellular, the new limitation of "an outside region of" cannot be used to exclude the prior art of record. The Examiner stated that the grounds of this rejection could be obviated by amending the claims to correspond to the language of page 54, line 5, which describes "an outer membrane domain[s]" of the PSM antigen.

In response, applicants respectfully traverse the Examiner's above rejection because an outside region is clearly synonymous with an outer membrane domain, both of which are synonymous with an extracellular domain. Nevertheless, applicants without conceding the correctness of the Examiner's position and without disclaimer or prejudice but to expedite prosecution of the subject application have hereinabove canceled claims 114-118 and 120-127 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in a later-filed application and added new claims 128-144. Newly added claims 128-139 recite the term "outer membrane domain." Horoszewicz discloses the 7E11-C5 antibody. As demonstrated in Figure 3 of Horoszewicz, the 7E11-C5 antibody binds to the inner-or cytoplasmic region of the PSMA antigen. In contrast, the now pending claims recite "an antibody which binds to

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 12

an outer membrane domain of prostate specific membrane antigen" [emphasis added]. Accordingly, Horoszewicz does not anticipate nor render obvious the claimed invention. Applicants contend that these amendments obviate this ground of rejection and respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §102(e).

Rejection under 35 U.S.C. §102(b)

The Examiner stated that claims 120-122 are rejected under 35 U.S.C. §102(b) as anticipated by Feng et al. (1991). The Examiner stated that Feng et al. discloses of an isolated PSM antigen with a molecular weight of 100 kds and a monoclonal antibody which reacts with said antigen.

The Examiner stated that applicant's arguments filed June 17, 2000 have been fully considered but they are not persuasive. The Examiner stated that applicant argues that the declarations of Kaladas, Rodwell, and Horoszewicz establish that the Feng reference is not enabling due to the lack of public availability of the 7E11-C5 hybridoma cell line. The Examiner stated that however, the 102(b) statute above clearly states that if the invention was described in a printed publication or in public use, the statute would apply. The Examiner stated that it is not required that the invention be described and be in public use. The Examiner stated that regarding applicant's arguments that the disclosure of the specific 7E11-C5 antibody should not anticipate a genus claim, since the Patent Office does not have the facilities for examining and comparing applicant's proteins with the proteins of the prior art reference, the burden is upon applicants to show an unobvious

I



Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 13

distinction between the material, structural and functional characteristics of the claimed proteins and the proteins of the prior art, citing In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

The Examiner stated that applicant's arguments and declarations filed March 2, 2000 have been fully considered but they are not persuasive because Applicant argues that 7E11-C5 and its antigen were not publicly available. The Examiner stated that however, the Examiner maintains the position that the instant invention was described in a printed publication which meets the statutory limitations.

The Examiner stated that applicant's arguments filed February 12, 2001 have been fully considered but they are not persuasive because the Examiner was unable to find a definition for "an outside region of" prostate specific membrane antigenic polypeptide in the specification. The Examiner stated that given the disclosure on pages 53-54 of only a membrane spanning domain, an "outside region" could be interpreted as being either the inner or outer membrane domain of the PSM antigen as described on page 54 because either domain is outside of the transmembrane domain which appears to be the only domain specifically identified in the specification, i.e. the Examiner could not find in the instant specification any teachings as to the orientation of the PSM antigen other than the disclosure of a membrane spanning domain. The Examiner stated that given the lack of teaching as the PSM antigen's orientation in the cell, i.e. to the location of the N-or C-terminal as being intracellular or extracellular, the new limitation of "an outside region of" cannot be used to exclude the prior art of record. The

I

Applicants: Ron S. Israeli et al.  
Serial NO.: 08/470,735  
Filed : June 6, 1995  
Page 14

Examiner stated that the grounds of this rejection could be obviated by amending the claims to correspond to the language of page 54, line 5, which describes "an outer membrane domain[s] of the PSM antigen."

In response, applicants respectfully traverse the Examiner's above rejection because an outside region is clearly synonymous with an outer membrane domain, both of which are synonymous with an extracellular domain. Nevertheless, applicants without conceding the correctness of the Examiner's position and without disclaimer or prejudice but to expedite prosecution of the subject application have hereinabove canceled claims 114-118 and 120-127 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in a later-filed application and added new claims 128-144. Newly added claims 128-139 recite the term "outer membrane domain" and not "outside region." Feng discloses the 7E11-C5 antibody. As stated supra on page 6, the 7E11-C5 antibody binds to the inner or cytoplasmic region of PSMA. In contrast, the now pending claims of the subject application recite an "antibody which binds to an outside region of prostate specific membrane antigen" [emphasis added]. Accordingly, Feng does not anticipate nor render obvious the claimed invention. Applicants contend that this amendment obviates the above ground of rejection and respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §102(b).

Allowable subject matter

Applicants hereby acknowledge the Examiner's indication of allowable subject matter.

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 14

Examiner stated that the grounds of this rejection could be obviated by amending the claims to correspond to the language of page 54, line 5, which describes "an outer membrane domain[s] of the PSM antigen."

In response, applicants respectfully traverse the Examiner's above rejection because an outside region is clearly synonymous with an outer membrane domain, both of which are synonymous with an extracellular domain. Nevertheless, applicants without conceding the correctness of the Examiner's position and without disclaimer or prejudice but to expedite prosecution of the subject application have hereinabove canceled claims 114-118 and 120-127 without disclaimer or prejudice to applicants' right to pursue the subject matter of these claims in a later-filed application and added new claims 128-144. Newly added claims 128-139 recite the term "outer membrane domain" and not "outside region." Feng discloses the 7E11-C5 antibody. As stated supra on page 6, the 7E11-C5 antibody binds to the inner or cytoplasmic region of PSMA. In contrast, the now pending claims of the subject application recite an "antibody which binds to an outside region of prostate specific membrane antigen" [emphasis added]. Accordingly, Feng does not anticipate nor render obvious the claimed invention. Applicants contend that this amendment obviates the above ground of rejection and respectfully request that the Examiner reconsider and withdraw the rejection under 35 U.S.C. §102(b).

Allowable subject matter

Applicants hereby acknowledge the Examiner's indication of allowable subject matter.

T

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 15

Summary

For the reasons set forth hereinabove, applicants respectfully request that the Examiner reconsider and withdraw the various grounds of objection and rejection and earnestly solicit allowance of the now pending claims, i.e. claims 128-144.

Applicant's Request for Interference

Pursuant to 37 C.F.R. §1.607, applicants hereby request an interference with U.S. Patent No. 6,107,090, issued August 22, 2000. A copy of this patent was submitted to the United States Patent Office in a Supplemental Information Disclosure Statement filed on October 20, 2000 in connection with the subject application. An additional copy of this patent was attached to the amendment filed on November 24, 2000.

Claim 25 of U.S. Patent No. 6,107,090 recites as follows:

An isolated antibody or antigen binding portion thereof which binds to an extracellular domain of prostate specific membrane antigen which binding occurs to living cells, wherein said antibody or antigen binding portion thereof is selected for its ability to bind to live cells.

New claim 137 of the subject application recites as follows:

A purified antibody which binds to an outer membrane

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 16

domain of prostate specific membrane antigen, the amino acid sequence of which antigen is set forth in SEQ ID NO:2.

Applicants hereby propose the following count for the interference:

Count I

An isolated antibody or antigen binding portion thereof which binds to an extracellular domain of prostate specific membrane antigen which binding occurs to living cells, wherein said antibody or antigen binding portion thereof is selected for its ability to bind to live cells; or a purified antibody which binds to an outer membrane domain of prostate specific membrane antigen, the amino acid sequence of which antigen is set forth in SEQ ID NO:2.

The proposed count is the antibody alternative of claim 25 of U.S. Patent No. 6,107,090 or claim 137 of the subject application. Claim 25 of the patent and claims 137 and 139 of the subject application correspond to the count. In addition, all of the claims of U.S. Patent No. 6,107,090, i.e. claims 1-24 and 26-60, in addition to claim 25 correspond to the count. In contrast, applicants' new claims 128-136, 138 and 140-144 do not correspond to the proposed count.

Pursuant to 37 C.F.R. §1.607(d) applicants specifically request that a notice be placed in the file of U.S. Patent No. 6,107,090 that applicants are seeking to provoke an interference with the

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 17

patent and that a copy of the notice be sent to the patentee.

Finally, pursuant to 37 C.F.R. §1.608, no prima facie showing is required by applicants since applicants' effective filing date is November 5, 1992 and the patent's earliest possible date is May 6, 1996. Therefore, applicants are also entitled to be designated the senior party in the interference.

Applicants are in compliance with 35 U.S.C. §135(b) since less than one year has elapsed since the issuance of U.S. Patent No. 6,107,090. Moreover, claims which recited "substantially the same subject matter" as those in the patent were pending in the subject application prior to the issuance of the patent.

If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorneys invites the Examiner to telephone either of them at the number provided below.

I

Applicants: Ron S. Israeli et al.  
Serial No.: 08/470,735  
Filed : June 6, 1995  
Page 18

No fee, other than the \$160.00 fee for additional claims is deemed necessary in connection with the filing of this Substitute Amendment and authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



John P. White  
Registration No. 28,678  
Spencer H. Schneider  
Registration No. 45,923  
Attorneys for Applicant(s)  
Cooper & Dunham, LLP  
1185 Avenue of the Americas  
New York, New York 10036  
(212) 278-0400

1